PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference PC-2001358	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/SE00/01135	International filing date *(day/month/year)* 31.05.2000	Priority date *(day/month/year)* 03.06.1999
International Patent Classification (IPC) or national classification and IPC7 C07K 14/705, A61K 38/17, C07K 16/28		
Applicant Active Biotech AB et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 14 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
21.12.2000	10.10.2001
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. 08-667 72 88	Authorized officer Hampus Rystedt/BS Telephone No. 08-782 25 00

Form PCT/IPEA/409 (cover sheet) (January 1998)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/SE00/01135

I. Basis of the report

1. With regard to the **elements** of the international application:*

☐ the international application as originally filed

☒ the description:
pages 1-36 , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the claims:
pages _____ , as originally filed
pages _____ , as amended (together with any statement) under article 19
pages _____ , filed with the demand
pages 37-50 , filed with the letter of 2001.09.11

☒ the drawings:
pages 1-9 , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

☒ the sequence listing part of the description:
pages 1-10 , as originally filed
pages _____ , filed with the demand
pages _____ , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☒ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, Nos. _____

☐ the drawings, sheet/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2 (c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item I and annexed to this report.*

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 2, 4, 12, 21, 29-40, 44-62, 65-82, 85-90, 96, 97, 101-103 partially and 42-43, 63-64, 83-84, 95 and 104-105 completely

because:

☒ the said international application, or the said claims Nos. 2,4, 30-40, 44-61, 65-82, 85-90, 96, 97, 101-103 partially and 42-43, 63-64, 83-84, 95 and 104-105 completely, relate to the following subject matter which does not require an international preliminary examination *(specify)*:

Claims 2 and 4 cover transgenic production in humans, which in many countries is considered unethical.

Claims 30-40, 44-61, 65-82, 85-90, 96, 97, 101-103 partially and 42-43, 63-64, 83-84, 95 and 104-105 completely, relate to methods of treatment of the human or animal body by therapy or diagnostic methods practised on the human or animal body. See PCT Rule 67.1. (iv).

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 12,21,29,50-70, 96 (partially) are so unclear that no meaningful opinion could be formed *(specify)*:

Claims 12, 21, 29, 50-70 and 96 (partially) relates to a binding entity specific to α11 integrin or homologues or fragments thereof. The wording "binding entities" is too broad to permit a meningful search, i.e. claims directed to these entities fail to comply with PCT Article 6. The search has been limited to antibodies directed towards α11 integrins.

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 12,21,29,50-70, 96 (partially)

see above

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

INTERNATIONAL PRE[redacted]NARY EXAMINATION REPORT

International application No.
[redacted]/SE00/01135

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	22-29,44-47,65-68,85-88	YES
	Claims	1-21,30-41,48-62,69-82,89-94,96-103	NO
Inventive step (IS)	Claims	22-29,44-47,65-68,85-88	YES
	Claims	1-21,30-41,48-62,69-82,89-94,96-103	NO
Industrial applicability (IA)	Claims	1-41,44-62,65-82,85-94,96-103	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

The claimed invention relates to a novel α-integrin subunit denoted α11.

The following documents are considered relevant:
D1) Genini M et al., "Isolation of genes differentially expressed in human primary myoblasts and embryonal rhabdomyosarcoma", Medline Accession no:96213800, GenBANK Accession Z50167 & 1996, vol. 66, page 571-577, International Journal of Cancer.

D2) Gullberg et al., "Up-regulation of a novel integrin α-chain (α_{mt}) on human fetal myotubes, 1995, vol. 204, page 57-65, Developmental Dynamics.

D3) WO92/19647

D4) Camper L et al., "Isolation and cloning and sequence analysis of the integrin subunit alpha-10, a beta associated collagen binding integrin expressed in chondrocyted", 1998, vol 273(32), pages 20363-20389.

D5) WPI-abstract 1997-297879&WO97/18838

D1 discloses a study of genes expressed in myoblasts but not in rhabdomyosarcoma in order to identify genes of interest in the development of neoplasia. D1 identifies a clone being 98% homologous with the present SEQ ID NO 1, between bp 298-643. This clone is suspected to encode an I-domain of a novel integrin. To produce an amino acid fragment from this clone, and direct an antibody against that fragment, is considered obvious to a person skilled in the art e.g. since it could have a role in the determination of a normal phenotype.

.../...

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Box V

D2 describes the α11-integrin. It is stated that the characterisation of the proteins stems from the limited availability of material. The purification of the protein does not seem to be a problem.

α-integrins are well-known in the art refer to D3-D5. The same applies for different aspects of the present application such as: recombinant production together with α-integrins, antibodies directed towards α-integrins and α-integrins as vaccine (D5).

Due to the broad wording, e.g. "the amino acid sequence shown in SEQ ID No. 1, and homologues and fragments thereof", in claims 1-21, 30-41, 48-62, 69-82, 89-94 and 96-103, the subject matter of these claims lack novelty. Neither the claims, nor the description, clearly disclose any special technical features but that of an α-integrin, that should be retained in the homologues or fragments claimed. Therefore, all α-integrins could be considered as homologous to present SEQ ID No. 1, and claims 1-21, 30-41, 48-62, 69-82, 89-94 and 96-103 lack novelty.

The α-integrin of the present application seems to have structural and biological features making this integrin unique. Thus, claims 22-29, 44-47, 65-68 and 85-88, which specify the features making the α11 integrin unique, are novel, industrially applicable and considered to involve an inventive step.

CLAIMS

1. A recombinant or isolated integrin subunit α11 comprising essentially the amino acid sequence shown in SEQ ID No. 1, and homologues and fragments thereof.

2. A process of producing a recombinant integrin subunit α11 comprising essentially the amino acid sequence shown in SEQ ID No. 1, and homologues and fragments thereof, which process comprises the steps of

a) isolating a polynucleotide comprising a nucleotide sequence coding for a integrin subunit α11, of for homologues and fragments thereof,

b) constructing an expression vector comprising the isolated polynucleotide,

c) transforming a host cell with said expression vector,

d) culturing said transformed host cell in a culture medium under conditions suitable for expression of said integrin subunit α11, of said homologues and fragments, in said transformed host cell, and, optionally,

e) isolating the integrin subunit α11, or homologues and fragments thereof, from said transformed host cell or said culture medium.

3. A process according to claim 2, step c, said transforming being an *in vitro* or *in situ* process.

4. A process according to claim 2, step c, said transforming being an *in vivo* process.

5. A process of providing an integrin subunit α11, of homolouges or fragments thereof, whereby said subunit is isolated from a cell in which it is naturally present.

6. An isolated polynucleotide or oligonucleotide comprising a nucleotide coding for an integrin subunit α11, or for homologues or fragments thereof, which polynucleotide or oligonucleotide comprises essentially the nucleotide sequence shown in SEQ ID No. 1 or suitable parts thereof.

7. An isolated polynucleotide or oligonucleotide which hybridises to a polynucleotide or oligonucleotide as defined in claim 4, whereby said isolated polynucleotide or oligonucleotide fails to hybridise to a polynucletide or oligonucleotide encoding an integrin subunit α10.

8. A vector comprising a polynucleotide or oligonucleotide as defined in claim 6 or 7.

9. A cell containing the vector as defined in claim 8.

10. A cell, as generated by the process in steps a) to c) of claim 2, in which a polynucleotide or oligonucleotide coding for an integrin subunit α11, or for homologues and fragments thereof, said polynucleotide or oligonucleotide comprising essentially the nucleotide sequence shown in SEQ ID No. 1 or parts thereof, has been stably integrated in the cell genome.

11. Binding sites of the amino acid sequence of the integrin subunit α11, or of homologues and fragments thereof, as defined in claim 1, said binding sites having the capability of binding specifically to entities chosen from the group comprising proteins, peptides, carbohydrates, lipids, natural integrin binding ligands, polyclonal and monoclonal antibodies, and fragments thereof.

12. Binding entities having the capability of binding specifically to integrin subunit α11, or to homologues or fragments thereof, as defined in claim 1, which entities are chosen from the group comprising proteins, peptides, carbohydrates, lipids, natural integrin binding ligands, polyclonal and monoclonal antibodies, and fragments thereof.

13. A recombinant or isolated integrin heterodimer comprising a subunit α11 and a subunit β, in which the subunit α11 comprises essentially the amino acid sequence shown in SEQ ID No. 1 or homologues or fragments thereof.

14. A recombinant or isolated integrin heterodimer according to claim 11, wherein the subunit β is β1.

15. A process of producing a recombinant integrin heterodimer comprising a subunit α11 and a subunit β, in which the subunit α11 comprises essentially the amino acid sequence shown in SEQ ID No. 1, or homologues or fragments thereof, which process comprises the steps of

a) isolating one polynucleotide or oligonucleotide comprising a nucleotide sequence coding for said subunit α11 of said integrin heterodimer, or for said homologues or fragments thereof, and, optionally, another polynucleotide comprising a nucleotide sequence coding for said subunit β of an integrin heterodimer, or for homologues or fragments thereof,

b) constructing an expression vector comprising said isolated polynucleotides or oligonucleotides

c) transforming a host cell with said expression vector or vectors,

d) culturing said transformed host cell in a culture medium under conditions suitable for expression of said integrin heterodimer, or said homologues or fragments thereof, in said transformed host cell, and, optionally,

e) isolating said integrin heterodimer, or said homologues or fragments thereof, from said transformed host cell or said culture medium.

16. A process according to claim 15, step c, said transforming being an *in vitro* process.

17. A process according to claim 15, step c, said transforming being an *in vivo* process.

18. A process of providing an integrin heterodimer comprising a subunit α11 and a subunit β, as defined in claim 13 or 14, or homologues or fragments thereof, whereby said integrin heterodimer is isolated from a cell in which it is naturally present.

19. A cell containing

i) a first vector, said first vector comprising a polynucleotide or oligonucleotide coding for a subunit

α11 of an integrin heterodimer, or for homologues or fragments thereof, which polynucleotide or oligonucleotide comprises essentially the nucleotide sequence shown in SEQ ID No. 1 or parts thereof, and

ii) a second vector, said second vector comprising a polynucleotide or oligonucleotide coding for a subunit β of said integrin heterodimer.

20. Binding sites of an integrin heterodimer as defined in claim 13 or 14, or of homologues or fragments thereof, said binding sites having the capability of binding specifically to entities chosen among the group comprising proteins, peptides, carbohydrates, lipids, natural integrin binding ligands, polyclonal and monoclonal antibodies, and fragments thereof.

21. Binding entities having the capability of binding specifically to an integrin heterodimer as defined in claim 13 or 14, or to homologues or fragments thereof, said binding entities being chosen among the group comprising proteins, peptides, carbohydrates, lipids, natural integrin binding ligands, polyclonal and monoclonal antibodies, and fragments thereof.

22. A fragment of an integrin subunit α11, which integrin subunit α11 comprises essentially the amino acid sequence shown in SEQ ID NO: 1, said fragment being a peptide chosen from the group comprising peptides of the cytoplasmic domain, the I-domain and the extracellular extension region.

23. A fragment according to claim 22, said fragment being a peptide from the cytoplasmic domain comprising essentially the amino acid sequence KLGFFRSARRRREPGLDPTPKVLE.

24. A fragment according to claim 22, which is a peptide comprising essentially the amino acid sequence of the extracellular domain, from about amino acid No. 804 to about amino acid no. 826 of SEQ ID No. 1.

25. A fragment according to claim 22, which is a peptide comprising essentially the amino acid sequence of

the I-domain, from about amino acid No. 159 to about amino acid no. 355 of SEQ ID No. 1.

26. A method of producing a fragment of the integrin subunit α11 as defined in any one of claims 22-25, which method comprises a sequential addition of amino acids.

27. A polynucleotide or oligonucleotide coding for a fragment of the integrin subunit α11 as defined in any one of claims 22-25.

28. Binding sites of an integrin subunit α11 fragment as defined in any one of claims 22-25, said binding sites having the capability of binding specifically to entities chosen from the group comprising proteins, peptides, carbohydrates, lipids, natural integrin binding ligands, monoclonal and polyclonal antibodies, and fragments thereof.

29. Binding entities having the capability of binding specifically to an integrin subunit α11 fragment as defined in any one of claims 22-25, which binding entities are chosen from the group comprising proteins, peptides, carbohydrates, lipids, natural integrin binding ligands, monoclonal and polyclonal antibodies, and fragments thereof.

30. A process of using an integrin subunit α11 comprising essentially the amino acid sequence shown in SEQ ID No.1 or an integrin heterodimer comprising said subunit α11 and a subunit β, or homologues or fragments thereof, as a marker or target molecule of cells or tissues expressing said integrin subunit α11, which cells or tissues are of animal including human origin.

31. A process according to claim 30, which is a process for determining the differentiation-state of cells during differentiation, development, in pathological conditions, in tissue regeneration, in transplantation, or in therapeutic and physiological reparation of tissues.

32. A process according to claim 31, which process is used during pathological conditions involving said subunit α11.

33. A process according to claim 31, which pathological conditions are comprised within the group comprising damage of muscles, muscle dystrophy, fibrosis and wound healing.

34. A process according to claim 31, which pathological conditions are comprised within the group comprising damage of cartilage and/or bone, and cartilage and/or bone diseases.

35. A process according to claim 31, which pathological conditions are comprised within the group comprising trauma, rheumatoid arthritis, osteoarthritis and osteoporosis.

36. A process according to claim 30, which is a process for detecting the formation of cartilage during embryonic development.

37. A process according to claim 30, which is a process for detecting physiological or therapeutic repair of cartilage and/or muscle.

38. A process according to claim 30, which is a process for selection and analysis, or for sorting, isolating or purification of chondrocytes and/or muscle cells.

39. A process according to claim 30, which is a process for detecting regeneration of cartilage or chondrocytes during transplantation of cartilage or chondrocytes, respectively, or of muscle or muscle cells during transplantation of muscle or muscle cells, respectively.

40. A process according to claim 30, which is a process for studies of differentiation of chondrocytes or muscle cells.

41. A process according to any one of claims 30-40, which is an *in vitro* process.

42. A process according to any one of claims 30-40, which is an *in situ* process.

43. A process according to any one of claims 30-40, which is an *in vivo* process.

44. A process according to any one of claims 30-43, whereby a fragment of said integrin subunit α11 is a peptide chosen from the group comprising peptides of the cytoplasmic domain, the I-domain and the extracellular extension region.

45. A process according to claim 44, whereby said fragment is a peptide comprising essentially the amino acid sequence KLGFFRSARRRREPGLDPTPKVLE from the cytoplasmic domain.

46. A process according to claim 44, whereby said fragment is a peptide comprising essentially the amino acid sequence of the extracellular domain, from about amino acid No. 804 to about amino acid no. 826 of SEQ ID No. 1.

47. A process according to claim 44, whereby said fragment is a peptide comprising essentially the amino acid sequence of the I-domain, from about amino acid No. 159 to about amino acid no. 355 of SEQ ID No. 1.

48. A process according to any one of claims 30-47, whereby a subunit β of the integrin heterodimer is β1.

49. A process according to claim 30, whereby said cells are chosen from the group comprising fibroblasts, muscle cells, chondrocytes, osteoblasts, mesenchymally derived cells and stem cells.

50. A process of using binding entities having the capability of binding specifically to binding sites of an integrin subunit α11 comprising essentially the amino acid sequence shown in SEQ ID No. 1, or an integrin heterodimer comprising said subunit α11 and a subunit β, or to homologues or fragments thereof, as markers or target molecules of cells or tissues expressing said integrin subunit α11, which cells or tissues are of animal including human origin.

51. A process according to claim 50, which is a process for detecting the presence of an integrin subunit α11 comprising essentially the amino acid sequence shown in SEQ ID No. 1, or of an integrin heterodimer comprising said subunit α11 and a subunit β, or of homologues or fragments thereof.

52. A process according to claim 50, which is a process for determining the differentiation-state of cells during differentiation, development, in pathological conditions, in tissue regeneration, in transplantation, or in therapeutic and physiological repair of tissues.

53. A process according to claim 52, which process is used during pathological conditions involving said subunit α11.

54. A process according to claim 52, which pathological conditions are comprised within the group comprising damage of muscles, muscle dystrophy, fibrosis and wound healing.

55. A process according to claim 52, which pathological conditions are comprised within the group comprising damage of cartilage and/or bone, and cartilage and/or bone diseases.

56. A process according to claim 52, which pathological conditions are comprised within the group comprising trauma, rheumatoid arthritis, osteoarthritis and osteoporosis.

57. A process according to claim 52 which is a process for detecting the formation of cartilage during embryonic development.

58. A process according to claim 52, which is a process for detecting physiological or therapeutic reparation of cartilage and/or muscle.

59. A process according to claim 52, which is a process for selection and analysis, or for sorting, isolating or purification of chondrocytes and/or muscle cells.

60. A process according to claim 52, which is a process for detecting regeneration of cartilage or chondrocytes during transplantation of cartilage or chondrocytes, respectively, or of muscle or muscle cells during transplantation of muscle or muscle cells, respectively.

61. A process according to claim 52, which is a process for studies of differentiation of chondrocytes or muscle cells.

62. A process according to any one of claims 50-61, which is an *in vitro* process.

63. A process according to any one of claims 50-61, which is an *in situ* process.

64. A process according to any one of claims 50-61, which is an *in vivo* process.

65. A process according to any one of claims 50-61, whereby a fragment of said integrin subunit α11 is a peptide chosen from the group comprising peptides of the cytoplasmic domain, the I-domain and the extracellular extension region.

66. A process according to claim 65, whereby said fragment is a peptide comprising essentially the amino acid sequence KLGFFRSARRRREPGLDPTPKVLE from the cytoplasmic domain.

67. A process according to claim 65, whereby said fragment is a peptide comprising essentially the amino acid sequence of the extracellular domain, from about amino acid No. 804 to about amino acid no. 826 of SEQ ID No. 1.

68. A process according to claim 65, whereby said fragment is a peptide comprising essentially the amino acid sequence of the I-domain, from about amino acid No. 159 to about amino acid no. 355 of SEQ ID No. 1.

69. A process according to any one of claims 50-68, whereby a subunit β of the integrin heterodimer is β1.

70. A process according to claim 50, whereby said cells are chosen from the group comprising fibroblasts,

muscle cells, chondrocytes, osteoblasts, mesenchymally derived cells and stem cells.

71. A process for detecting the presence of an integrin subunit α11, or of homologues or fragments of said integrin subunit, on cells, whereby a polynucleotide or oligonucleotide chosen from the group comprising a polynucleotide or oligonucleotide having essentially the nucleotide sequence as shown in SEQ ID No. 1, or homologues or fragments thereof, is used as a marker under hybridisation conditions, wherein said polynucleotide or oligonucleotide fails to hybridise to a polynucleotide or oligonucleotide encoding an integrin subunit α10.

72. A process according to claim 71, which is a process for determining the differentiation-state of cells during differentiation, development, in pathological conditions, in tissue regeneration, in transplantation, or in therapeutic and physiological reparation of tissues.

73. A process according to claim 72, which process is used during pathological conditions involving said subunit α11.

74. A process according to claim 72, which pathological conditions are comprised within the group comprising damage of muscles, muscle dystrophy, fibrosis and wound healing.

75. A process according to claim 72, which pathological conditions are comprised within the group comprising damage of cartilage and/or bone, and cartilage and/or bone diseases.

76. A process according to claim 72, which pathological conditions are comprised within the group comprising trauma, rheumatoid arthritis, osteoarthritis and osteoporosis.

77. A process according to claim 72, which is a process for detecting the formation of cartilage during embryonic development.

78. A process according to claim 72, which is a process for detecting physiological or therapeutic reparation of cartilage and/or muscle.

79. A process according to claim 72, which is a process for selection and analysis, or for sorting, isolating or purification of chondrocytes and/or muscle cells.

80. A process according to claim 72, which is a process for detecting regeneration of cartilage or chondrocytes during transplantation of cartilage or chondrocytes, respectively, or of muscle or muscle cells during transplantation of muscle or muscle cells, respectively.

81. A process according to claim 72, which is a process for studies of differentiation of chondrocytes or muscle cells.

82. A process according to any one of claims 71-81, which is an *in vitro* process.

83. A process according to any one of claims 71-81, which is an *in situ* process.

84. A process according to any one of claims 71-81, which is an *in vivo* process.

85. A process according to any one of claims 71-84, whereby said polynucleotide or oligonucleotide is a polynucleotide or oligonucleotide coding for a peptide chosen from the group comprising peptides of the cytoplasmic domain, the I-domain and the extracellular extension region.

86. A process according to claim 85, whereby said peptide is a peptide comprising essentially the amino acid sequence KLGFFRSARRRREPGLDPTPKVLE from the cytoplasmic domain.

87. A process according to claim 85, whereby said peptide is a peptide comprising essentially the amino acid sequence of the extracellular domain, from about amino acid No. 804 to about amino acid no. 826 of SEQ ID No. 1.

88. A process according to claim 85, whereby said peptide is a peptide comprising essentially the amino acid sequence of the I-domain, from about amino acid No. 159 to about amino acid no. 355 of SEQ ID No. 1.

89. A process according to any one of claims 71-88, whereby a subunit β of the integrin heterodimer is β1.

90. A process according to claim 71, whereby said cells are chosen from the group comprising fibroblasts, muscle cells, chondrocytes, osteoblasts, mesenchymally derived cells and stem cells.

91. A pharmaceutical composition comprising as an active ingredient a pharmaceutical agent or an antibody which is capable of using an integrin heterodimer comprising a subunit α11 and a subunit β, or the subunit α11 thereof, or homologues or fragment of said integrin or subunit α11, as a target molecule.

92. A pharmaceutical composition comprising as an active ingredient a pharmaceutical agent or an antibody which is capable of stimulating cell surface expression or activation of an integrin heterodimer comprising a subunit α11 and a subunit β, or the subunit α11 thereof, or homologues or fragmens of said integrin or subunit α11.

93. A pharmaceutical composition according to claim 92, for use in stimulating, inhibiting or blocking the formation of muscles, cartilage, bone or blood vessels.

94. A vaccine comprising as an active ingredient at least one member of the group comprising an integrin heterodimer, which heterodimer comprises a subunit α11 and a subunit β, or the subunit α11 thereof, and mologues or fragments of said integrin or subunit α11, and a polynucleotide and a oligonucleotide coding for said integrin subunit α11.

95. A method of gene therapy, whereby a vector comprising a polynucleotide or oligonucleotide coding for a subunit α11 of an integrin heterodimer, or for homologues or fragments thereof, which polynucleotide or

oligonucleotide comprises essentially the nucleotide sequence shown in SEQ ID NO: 1 or parts thereof, and optionally a second vector comprising a polynucleotide or oligonucleotide coding for a sbunit β of said integrin heterodimer, is administered to a subject suffering from pathological conditions involving said subunit α11.

96. A method of using binding entities having the capability of binding specifically to binding sites of a integrin subunit α11 comprising substantially the amino acid sequence shown in SEQ ID No. 1, or of an integrin heterodimer comprising said subunit α11 and a subunit β, or to homologues or fragments thereof, for promoting adhesion of cells.

97. A method of using an integrin heterodimer comprising an integrin subunit α11 and a subunit β, or the subunit α11 thereof, or homologues or fragments of said integrin or subunit α11, as a target for anti-adhesive drugs or molecules in tissues where adhesion impairs the function of the tissue.

98. A method of in vitro detecting the presence of integrin binding entities, comprising interaction of an integrin heterodimer comprising a subunit α11 and a sub-unit β, or the subunit α11 thereof, or homologues or fragments of said integrin or subunit, with a sample, thereby causing said integrin, subunit α11, or homologue or fragment thereof, to modulate the binding to its natural ligand or other integrin binding proteins present in said sample.

99. A method of in vitro studying consequences of the interaction of a human heterodimer integrin comprising a subunit α11 and a subunit β, or the subunit α11 thereof, or homologues or fragments of said integrin or subunit, with an integrin binding entity and thereby initiate a cellular reaction.

100. A method according to claim 99, whereby the consequences of said interactions are measured as alterations in cellular functions.

101. A method of using a polynucleotide or oligonucleotide encoding an integrin subunit α11 or homologues or fragments thereof as a target molecule.

102. A method according to claim 101, comprising hybridising a polynucleotide or oligonucleotide to the DNA or RNA encoding the integrin subunit α11 or homologue or fragment thereof, which polynucleotide or oligonucleotide fails to hybridise to a polynucleotide or oligonucleotide encoding an integrin subunit α10.

103. A method of using binding entities having the capability of binding specifically to an integrin subunit α10 comprising the amino acid sequence shown in SEQ ID No. 1 or SEQ ID No. 2, or an integrin heterodimer comprising said subunit α10 and a subunit β, or to homologues or fragments thereof having similar biological activity, for promoting adhesion of chondrocytes and/or osteoblasts to surfaces of implants to stimulate osseointegration.

104. A method of using an integrin heterodimer comprising an integrin subunit α11 and a subunit β, or the subunit α10 thereof, or homologues or fragments of said integrin or subunit α10, as a target for anti-adhesive drugs or molecules in tendon, ligament, skeletal muscle or other tissues where adhesion impairs the function of the tissue.

105. A method of stimulating, inhibiting or blocking the formation of cartilage or bone, comprising administration to a subject a suitable amount of a pharmaceutical agent or an antibody which is capable of using an integrin heterodimer comprising a subunit α11 and a subunit β, or the subunit α11 thereof, or homologues or fragments of said integrin or subunit α11, as a target molecule.